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PUBLIC HEALTH REPORTS.

VOL. XXVI.

MARCH 17, 1911.

No. 11.

THE TYPHOID BACILLUS "CARRIER": A REVIEW.

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The article of which this review is a brief abstract is a report on the typhoid bacillus carrier, and is a review of the current knowledge on this subject. It is written by Dr. J. C. G. Ledingham, and occurs in the supplement to the thirty-ninth annual report of the local government board of England and Wales for the year 1909-10 containing the report of the medical officer. It consists of 15 chapters, in which the author reviews numerous reports by various writers and in which he reports some of his own observations. The subjects taken up are as follows: General facts regarding carriers, with reference to age, sex, frequency, etc.; pathogenesis of the carrier state; physical disabilities; intestinal carriers, treatment; urinary carriers, treatment; diagnostic methods employed; general questions of infectivity, statistical data; immunity, and various measures employed or suggested to diminish the spread of typhoid by carriers. Four chapters are devoted to accounts of instances of the infectivity of carriers. House and street cases, milk-borne cases, institutional cases, and army cases are taken up. A bibliography of 186 references is given at the end. For the purposes of this article a slightly different arrangement of subjects has been made, but in general the outline of the memoir has been followed.

INTRODUCTORY.

In the introductory chapter the author states that in the memoir he is "concerned solely with the typhoid bacillus and its recently recognized property of leading a saprophytic existence in an organism which may or may not react to its presence in any obvious fashion." He lays great stress on the important rôle played by the "carrier" and practically agrees with Frosch in his statement that if we can cure the typhoid bacillus carrier we can get rid of typhoid fever.

To Koch is given the credit of pointing out the necessity of supervision of typhoid cases, of typhoid convalescents, and of ambulant and abortive cases. It was upon Koch's recommendation that

bacteriological stations were established in southwest Germany for the study of typhoid fever, and since many of the reports from these stations have been used by the author in his memoir he gives a brief account of the organization of the German campaign.

The first experimental typhoid station of the German campaign was founded at Trier in 1903 under the directorship of Frosch. Later the number of stations was increased to 11, located at different places in southwest Germany. The typhoid stations are provincial establishments. Each laboratory has a director, two or three bacteriologists, and several attendants. The workers at each laboratory work in conjunction with the local authorities and have a fourfold duty, as follows:

1. To assist the local physicians in the diagnosis of typhoid fever.
2. To ascertain the source of infection in typhoid cases and render it innocuous, and to seek out infected persons.
3. To watch for unhygienic conditions and to make recommendations concerning them.
4. To make bacteriological examinations of stools and urine in order to determine when convalescents cease eliminating typhoid bacilli.

The workers at these laboratories have added and are still adding a great deal to our recent knowledge on the subject of typhoid fever and of the typhoid bacillus carrier.

GENERAL FACTS REGARDING CARRIERS.

1. *Elimination of typhoid bacilli during the course of the disease.*—Some statistics by different writers on this subject are given and, although the findings vary somewhat, they are all very significant.

(a) Drigalski followed 64 cases, with the following result:

Time.	Typhoid bacilli present in stools.	Percent- age.
Cases.		
First to fifth day of disease	10	15.6
Sixth to tenth day of disease	15	23.4
Eleventh to twentieth day of disease	21	33
Twenty-first to twenty-seventh day of disease	8	11.5
After 8 to 10 weeks	7	11
After 3 months and later	3	4.7

(b) Brion and Kayser examined 144 cases during the febrile period with the following result:

Time.	Cases exam- ined.	Positive.
		Per cent.
First week of disease	22	32
Second week of disease	51	35
Third week of disease	71	45

(c) Bohne reports on a small series of 27 cases and finds the highest percentage during the fourth week:

Time.	Cases examined.	Positive.
First week of disease	2	0
Second week of disease	13	23
Third week of disease	7	43
Fourth week of disease	4	100
Fifth week of disease	1	(1)

¹ 1 case.

(d) The most trustworthy results obtainable are probably those of Gaehtgens and Brückner, from a series of 72 cases, where the more recently introduced methods were used. Their findings follow:

Time.	Cases examined.	Positive.
First week of disease	21	57
Second week of disease	32	53
Third week of disease	13	77
Fourth week of disease	4	50
Fifth week of disease	2	(2)

² 2 cases.

From the above findings it appears most likely that it is during the third week of the disease that the highest percentage of typhoid cases eliminate typhoid bacilli in the feces. Most observers agree that in about 25 per cent of typhoid cases typhoid bacilli can be demonstrated in the urine. This bacilluria usually occurs during the later stages of the disease, after defervescence or during late convalescence, although it may occur at the time of the eruption of the rose spots.

2. *Classification of carriers.*—In any clear discussion of the carrier some sort of classification is evidently necessary, since much confusion exists in the literature for want of a uniform classification for carriers. Several classifications are given which must necessarily be more or less artificial and not applicable to every case, because it is not possible to obtain in each case the data necessary for classifying it.

(a) Conradi has adopted the following classification:

First group.—Primary carriers: Those carriers in whom the infection has not led to symptoms, including persons in the incubation stage of the disease.

Second group.—Secondary carriers: Convalescents from typhoid fever who continue to eliminate bacilli for a period longer than 10 weeks after the onset of the attack.

Third group.—Tertiary carriers: Those carriers who continuously eliminate bacilli after the primary attack.

(b) Sacquepée has recently suggested a more intelligible and comprehensive classification.

Group 1.—Precocious carriers: Those carriers in the incubation stage of the disease.

Group 2.—Persons who have recovered from typhoid fever, but who continue to eliminate typhoid bacilli.

Subgroup A.—Convalescent carriers: Those who cease eliminating bacilli before the end of the third month.

Subgroup B.—Chronic carriers: Those who eliminate bacilli for an indefinite period.

Group 3.—Paradoxical carriers: Those who have never had symptoms of typhoid fever, but who eliminate bacilli for an indefinite period.

(c) For ordinary purposes, however, typhoid bacillus carriers may be classed into two great groups, "temporary" or "transitory" and "chronic" carriers. The terms "temporary" or "transitory" carriers (*bazillenträger* of the German writers) are applied to convalescents who cease eliminating typhoid bacilli before the end of the third month after the onset of the disease, while the term "chronic" carriers (*dauерträger* of the German writers) is applied to carriers who eliminate bacilli for an indefinite period.

3. *Frequency of carriers.*—Reports by various writers are considered by the author to give an idea as to the frequency of carriers. Great variation in results is found, which may be due to a number of factors, such as too few examinations in view of the prolonged periods of intermission of bacilli elimination, or to our bacteriological methods, which at best fall far short of being perfect in their application to the carrier problem.

Brief extracts from some of the reports are presented here:

(a) Lentz examined 400 convalescents and found 4.5 per cent carriers, 1.5 per cent temporary and 3 per cent chronic.

(b) Conradi examined 400 convalescents and found 6 per cent carriers, 5.5 per cent secondary (temporary) and 0.5 per cent tertiary (chronic).

(c) Klinger followed 482 cases of typhoid fever and found that 11.4 per cent eliminated bacilli during convalescence, but not longer than six weeks after defervescence, and 1.7 per cent longer than six weeks.

(d) Klinger, in another series of 604 convalescents, found 11.6 per cent temporary intestinal carriers, 1.7 per cent temporary urinary carriers, and 1 per cent chronic carriers. He states that all the urinary carriers were cured by urotropin.

(e) Kayser, in conjunction with Brion, obtained a carrier percentage of 1.5 in a series of 200 convalescents. In another series of 101 persons, who had previously been discharged as typhoid-free, he made examinations one year after their attack of typhoid fever and obtained a carrier percentage of 3. This shows the great importance of late control examinations.

(f) Brückner examined 316 persons who had had typhoid fever in previous years and found 3.8 per cent carriers; but, if only adults were considered, 5.2 per cent.

(g) Probably the most thorough work on this phase of the subject is that by Semple and Grieg, working in India. In their work, 86 typhoid convalescents were followed and bacteriological examinations of the excreta were made daily until the case could be classified. They found that of the 86 convalescents 11.6 per cent eliminated bacilli for a period longer than six weeks after defervescence, i. e., chronic carriers. This is undoubtedly the highest carrier percentage recorded and is probably due to the elaborate routine and thoroughness of the work.

(h) Aldridge, also in India, examined 190 typhoid convalescents in the army and found 3.1 per cent were eliminating typhoid bacilli longer than six months after defervescence.

(i) Tsuzuki examined 51 typhoid convalescents in the Japanese army and found that 5.8 per cent were eliminating typhoid bacilli beyond the three-month limit.

(j) From the statistics from the whole German campaign, in one series of 3,867 typhoid cases, a carrier percentage of 1 was obtained; in another series of 6,708 cases a chronic carrier percentage of 2.47 and a temporary carrier percentage of 2.15 were obtained. Several reports are given of attempts to obtain the carrier percentage among the general population where healthy persons only were examined.

(k) Klinger reports on the examination of the excreta of 1,700 persons living in the neighborhood of actual cases, where a carrier percentage of 0.88 was obtained.

(l) Rosenau, Lumsden, and Kastle report on the examination of 1,014 specimens of feces and 26 specimens of urine of persons living in Washington, D. C., where a carrier percentage of 0.3 was obtained; that is, 3 per 1,000.

(m) Minelli examined 250 persons in an institution situated in a town free of typhoid fever and obtained a carrier percentage of 0.5.

4. *Facts regarding age, sex, etc.*—(a) In 1909 Prigge reported on the examinations made at Saarbrücken during the three years previous. There were examined 10,481 persons and 84 carriers discovered, making a carrier percentage of 0.77. He took one year as the limit between the temporary and the chronic carriers, and classified them as follows:

A. Temporary carriers:

α. In the incubation stage, 3 persons.

β. Clinically cured, but eliminating bacilli from 10 weeks to 1 year, 25 persons—9 men and 16 women.

γ. Healthy persons, 24—16 men and 8 women.

B. Chronic carriers:

δ. Persons giving a typhoid history, 27.

ε. Persons giving no typhoid history, 8—all women.

In another series of 102 carriers, Prigge found 17 males and 85 females, a ratio of 1 to 5.

(b.) Many interesting points are found in the carrier statistics of the whole campaign conducted in southwest Germany from its commencement to the end of 1907. These have been fully worked up and commented upon by Klinger. Notification of 431 carriers had been made. The period of three months was taken as the upper limit for the transitory carrier. Of the 431 carriers, 220 were chronic and 211 were transitory. Of the chronic carriers, 80 per cent gave a history of an attack of typhoid fever, while of the transitory carriers only 43.6 per cent gave such a history. The ratio of females to males among the chronic carriers was 5 to 1, while among the transitory carriers it was only 1.4 to 1. The majority of the chronic carriers was among persons in middle age, the greatest number per five-year age group occurring in the group 40 to 45 years. The majority of the transitory carriers was among young persons, the greatest number occurring in the age group 5 to 10 years. These facts are shown in the memoir by means of a table and a chart, which are not reproduced here.

A definite diagnosis of gallstone disease was made in 13.6 per cent of the chronic cases. Of the chronic cases, 30 had their attack of typhoid fever from 4 to 30 years previously. In 42 of the chronic carriers a spontaneous cessation in the discharge of typhoid bacilli was noted, but these bacteriological cures should be regarded with great skepticism in view of the prolonged periods of intermission which have been found to occur in carriers.

(c) Frosch, in considering 6,708 cases of typhoid fever, found that 310 became carriers, 144 transitory, and 166 chronic. Females formed 80 per cent of the chronic carriers and 60 per cent of the transitory carriers. Children under 15 years of age formed only 4 per cent of the chronic carriers, but 35 per cent of the transitory carriers.

5. *Infant carriers.*—It is known that children form a small percentage of the chronic carriers, but their importance as transitory carriers has been repeatedly demonstrated. One interesting and instructive case is taken from a report by Rommeler, which at once illustrates the importance and danger of the carrier in the persons of young children.

The case cited is that of an 18-months-old suckling child, whose mother was taken ill with typhoid fever. The child was nursed by its mother for eight days after the onset of her illness and was then taken charge of by a neighbor. On the first day of her custody the foster mother noticed that the child had a slight diarrhea, which she attributed to the necessary weaning. Seventeen days later the foster mother developed typhoid fever. Within the next two months five other members of the household developed typhoid fever, one of whom died. Six weeks after the slight diarrhea of the child its stools were positive for typhoid bacilli on two different occasions, but negative on nine subsequent examinations. Its serum gave a positive Widal in a dilution of 1 in 100.

6. *"Precocious" carriers and early contact cases.*—The presence of typhoid bacilli in stools during the incubation stage has been demonstrated by a number of observers. G. Mayer, in 1903, found typhoid bacilli in the stools of a boy who did not develop symptoms until eight days later. Other cases have been reported by Conradi and Klinger. Tables are given in the memoir taken from a report by Conradi which show the high degree of infectivity of persons in the first weeks of the disease. Another table, compiled by Klinger, shows the same and in addition the infectivity of persons in the incubation period of the disease. It is unfortunate that the period of highest infectivity should occur at the stage of the disease when few or no precautions are being taken.

(a) A summary of Conradi's tables is given here, which shows his findings in 85 cases of secondary infection, where the primary case was known and where the time of exposure was pretty definitely determined.

	Time.	Number of cases.
Secondary cases infected by primary case.....	First week of disease.....	49
Do.....	Second week of disease.....	16
Do.....	Third week of disease.....	10
Do.....	Fourth week of disease.....	5
Do.....	Fifth week of disease.....	3
Do.....	Sixth week of disease.....	1
	Seventh week of disease.....	1

From this table it is seen that about 58 per cent of these contact cases took place during the first week of the disease, but Conradi thinks that some of these may have become infected during the incubation period of the primary case.

(b) Klinger's table is based on 812 contact infections, and shows what an important source of infection an early typhoid case is. In 60 of these cases the incubation period was pretty definitely determined and found to vary from 5 to 45 days, with an average of 16 days. In his table the incubation period is taken as two weeks.

	Time.	Number of cases.
Secondary cases infected by primary case.....		
Do.....	First week of incubation period.....	33
Do.....	Second week of incubation period.....	150
Do.....	First week of disease.....	187
Do.....	Second week of disease.....	158
Do.....	Third week of disease.....	116
Do.....	Fourth week of disease.....	59
Do.....	Fifth week of disease.....	34
Do.....	Sixth week of disease.....	22
Do.....	Seventh week of disease.....	14
Do.....	Eighth week of disease.....	16
Do.....	Ninth week of disease.....	15
Do.....	Tenth week of disease.....	8

This table shows that a typhoid case is most dangerous for others during the incubation period and during the first few weeks of the disease. The precautions which are usually taken, and also the decrease in the elimination of bacilli during the later weeks, evidently serve to keep down the number of secondary infections during this period.

INTESTINAL CARRIERS.

1. *Pathogenesis of the carrier state:* (a) Many years before the recognition of the typhoid bacillus carrier it was known that typhoid bacilli could be isolated from the bile and from the upper portions of the intestinal tract of persons dead of typhoid fever. It was also known that typhoid bacilli could be isolated from the contents of the gall bladder and from the interior of gall stones of some cases coming to operation for cholelithiasis. One such case was reported by Droba in 1899, where there was a history of typhoid fever 17 years before, and another one by Cushing, in 1898, where no history of typhoid fever was obtained. Short accounts of reports of similar cases are given, but in a few of them only is there any note on the bacteriological examination of the stools and urine. In these few cases the number of stool examinations was limited and no conclusions were drawn regarding the elimination of typhoid bacilli. Since the recognition of the carrier, bacteriological examinations of stools and urine have been made more frequently and with greater care.

(b) *Relation of the carrier to the gall bladder.*—It is known that many carriers suffer from gall stones, and that many others show a condition of cholelithiasis at operation or at autopsy, even though they may not have had symptoms pointing to this condition. In 1892 Naunyn noted the frequency of gall stones in persons with a typhoid fever history, but Forster, in 1908, first directed attention to the association of gall-bladder troubles with typhoid carriers. A number of cases are cited by the author, which show the important relation of the gall bladder to the carrier state.

The percentage of carriers who have symptoms referable to the gall bladder is much higher among chronic than among transitory carriers. Of 220 chronic carriers reported by Klinger 13.6 per cent allowed a definite diagnosis of gall stones to be made. This corresponds closely to the 10 per cent of gall-stone cases of all origin that present diagnostic symptoms. Forster reports that in a series of 173 chronic carriers who were eliminating typhoid bacilli from 1 to 30 years after their primary attack, the ratio of females to males was 5 to 1. This corresponds closely to the ratio of gall-stone incidence in the female to that in the male, which is about 3 to 1.

(c) The relation of the typhoid bacillus to gall stones of chronic carriers has given rise to much discussion. The question at issue is whether the bacilli favor stone formation by merely forming a nucleus or otherwise, or whether the bacilli enter the preformed stone. Bachmeister thinks that recently formed stones are generally sterile and that only old stones contain bacilli, while Cushing thinks that only recently formed stones contain bacilli. Reports of experiments are given where *B. coli* and *B. typhosus* have been recovered from the center of cholesterin gall stones after the stones had been allowed to remain in broth cultures of these organisms. Similar results were not obtained with other kinds of stones. The author aptly notes that nothing is given of the histories of the persons furnishing the stones for these experiments.

Experimental results seem to leave no doubt that the typhoid bacillus may play some part in the formation of gallstones, but at the present time nothing definite can be said concerning its relative importance in this process.

(d) The relation of the typhoid bacillus to the gall bladder has been made more clear by animal experimentation and by microscopic examination of the walls of the gall bladder of infected persons. It has been found that after intravenous injections of typhoid bacilli into rabbits the gall bladder may harbor the organism for 109 days. In some cases the bacilli may be recovered from the gall bladder wall two hours after an intravenous injection. The observation has been made in these experiments that the bile may remain sterile and yet typhoid bacilli may be recovered from the mucosa of the gall bladder.

Doerr performed the following experiments: He demonstrated the presence of bacilli in the bile eight hours after an intravenous injection. In another animal he ligated the hepatic duct before injection and found that the bile [in the gall bladder?] remained sterile. He found also that when the cystic duct was ligated before injection, the bile remained sterile also. From these findings Doerr concluded that the bacilli came to the gall bladder by the bile route and not by its blood vessels. J. Koch has questioned Doerr's results, for in histological sections of the walls of the gall bladder of a person dead of typhoid fever he demonstrated small nests of typhoid bacilli in the mucosa of the gall bladder and found that these nests bore a close relationship to the small capillaries in the papillæ of the sub-mucosa. On account of these findings Koch suggests that typhoid bacilli reach the gall bladder by means of the blood vessels in its walls. Other workers also have questioned Doerr's results, so it is by no means definitely determined in what way typhoid bacilli reach the gall bladder.

(e) Many theories have been advanced to explain the carrier state. Forster reports a case of a man becoming a carrier after an attack of typhoid fever which came on two years after an operation for appendicitis. Forster suggests that in this case the altered circulatory conditions may have predisposed to the carrier state. Portal stasis, caused by tight corsets, frequent pregnancies, etc., has been advanced as an explanation of the preponderance of gallstones in the female and consequently may have some bearing on bringing about the carrier state in females. Lentz suggests that circulatory disturbances due to pregnancies and to overexertion in household work may be a factor. Prigge thinks that menstrual and puerperal blood losses should be considered. Fornet holds the view that the carrier state is due to an established immunity to the typhoid bacillus where the primary attack has brought about such a tolerance for the bacillus as to render possible its saprophytic existence in the body of the carrier. He thinks that a person becomes a carrier only after a second symptomless infection by an organism which may or may not be descended from the one causing the primary infection. He has compiled statistics to support this view.

2. *Treatment of intestinal carriers.*—The treatment of typhoid bacillus carriers has been far from satisfactory. Up to the present time no sure method has been found for rendering the carrier typhoid free. "Spontaneous" cures have been reported, but these results have to be accepted with great caution in view of the prolonged period of intermission of bacilli elimination in some carriers and on account of the fact that bacteriological methods fall far short of perfection at the present time. Minimal quantities of typhoid bacilli in a stool may easily escape detection when only a small proportion of it is used in an examination.

Many drugs have been tried and found wanting. Salol, betanaphthol, calomel, bile and its salts, turpentine oil, sodium bicarbonate, chloroform, and other drugs have only a temporary effect in decreasing the elimination of typhoid bacilli in the stools. One "cure" is claimed for sodium salicylate, where 3 to 5 grams were given daily at intervals for over a year. Lactic acid bacilli have been given with questionable results.

The surgical measures for the cure of carriers have been directed chiefly toward the gall bladder as the main seat of vegetation of the bacilli. The author reviews a number of reported cases in which the gall bladder was either drained or removed. In general the results obtained were by no means encouraging. When it is recalled that at autopsy of carriers typhoid bacilli have been recovered from the liver, walls of the gall bladder, from the large bile ducts, mesenteric glands, and other organs, the difficulty of the situation is at once apparent.

Typhoid vaccines and exposure of the gall bladder region to the X-ray have been tried, but promise little. G. Mayer has recommended an exclusive milk diet during the course of the disease and during convalescence as being less favorable to carrier production than is a mixed diet. The use of salicylates is the only means recommended by the author for arresting or diminishing the invasion of the bile tracts by typhoid bacilli during the course of the disease.

URINARY CARRIERS.

1. *Occurrence.*—The urinary carrier is not so frequently discovered as is the intestinal carrier. The great majority of chronic carriers discovered have eliminated bacilli in the feces only. In many of the female urinary carriers reported, the urine was probably contaminated with feces, for in the few cases where catheterized specimens have been examined the urine has been found to be constantly negative. The author has never found the urine positive for typhoid bacilli in a male chronic carrier. It is not uncommon to find both the urine and the feces positive in transitory and in early convalescent carriers. Schneller reports transitory carriers with urine positive and feces negative, some with feces positive and urine negative, and others with both urine and feces positive. A number of other reports are reviewed which show that the true urinary carrier is an important factor in the carrier problem and should not be overlooked.

2. *Pathology.*—The pathology of the urinary carrier is by no means complete. Nephro-typhoid may be associated with fecal abscesses of the kidney, which may have a bearing. It is known that an inflamed or cystic renal pelvis is the main depot of the typhoid bacillus in urinary carriers, and this condition may or may not be associated with an inflamed bladder, which may act as a secondary depot. Existing inflammation of the urinary tract may predispose to the carrier state by serving as a favorable site for the lodging and vegetation of the bacilli, whence they may be discharged into the urine. Reports of cases are given which seem to substantiate these statements.

3. *Treatment of the urinary carrier.*—Urotropin has not proved so efficacious in the treatment of the bacilluria of carriers as in the treatment of the bacilluria of convalescence. The best that can be said for it is, that it does decrease the number of bacilli eliminated during its administration, but that they reappear in full force when the drug is suspended. Semple and Greig found urotropin of little or no service in their series. In a case reported by Niepratschk this drug was given a thorough trial with no permanent reduction of bacilli eliminated. Borovertin (hexamethylene tetramine triborate) was then tried in the same case with apparent success. Six grams were given daily for a month and seemed to have a remarkable disinfectant action on the urine. Niepratschk considered this case a "cure." One other "cure" with borovertin has been reported. The author thinks that borovertin should receive a thorough trial in the treatment of urinary carriers and should be given after a preliminary course of urotropin.

Treatment with vaccines from the homologous strain has met with some measure of success, especially when the urine has been made alkaline by the administration of sodium salicylate.

PHYSICAL DISABILITIES OF THE CARRIER STATE.

1. Aside from the gall-bladder symptoms, carriers are but little inconvenienced by the presence of typhoid bacilli in their bodies. Occasionally headaches are complained of, chiefly by the urinary carriers. G. Mayer has noted periodic intestinal disturbances in carriers, as in the early spring, midsummer, or late autumn. Carriers

of a nervous temperament may develop a form of neurosis on account of the knowledge of their condition, of which they are constantly reminded by the necessary precautions of disinfection which they have to take.

2. Several reports of fatal cases of autoinfection are reviewed where carriers apparently succumbed to a general infection by their own bacillus. Some of the cases were verified bacteriologically. Cases of autoinfection are usually fatal.

INSTANCES OF INFECTIVITY OF CARRIERS.

The author of the article reviews a great number of instances which have been reported in the literature by individual observers and by the workers in the campaign in southwest Germany. The cases are classified as house and street cases, milk-borne cases, institutional cases, and army cases, and a chapter is devoted to each class. Only a few of these cases can be reviewed here.

1. A case of a carrier in the person of a baker's wife has been reported by Kayser and is of interest. In May, 1904, an apprentice baker living with his master contracted typhoid fever and died. It was learned that the baker's wife had had typhoid fever some years before and also that practically every apprentice baker had become afflicted with some gastrointestinal disturbance soon after his term of service with this baker began. The wife said these symptoms were caused by "too good diet." The stools of the woman were examined and she was found to be a carrier. She was intractable and took no precautions. In the following August her tenant took sick and died of typhoid fever, and later one other case was attributed to her—three cases in all.

Kayser reports another instance where 4 cases were attributed to a female carrier who had had typhoid fever 40 years before.

An interesting case reported by Mayer is that of a manager of an estate who was found to be a carrier. The manager had suffered from typhoid fever 10 years before, and during these 10 years there had been 16 cases of typhoid fever on or near the estate. It was practically certain that the manager had been the source of these infections.

The well-known New York case, which has been reported by Soper, is of considerable interest. In this case the carrier was a cook, who infected 26 persons in 7 different families.

Many other instances of carriers are reviewed which can not be given here, but attention is called to the fact that many of them were "Hausfrauen," or persons who handled food; cooks, boarding-house keepers, etc. The statistics of Frosch show the importance of this class of carriers, for among 454 female carriers reported by him there were 314 "Hausfrauen" and 56 domestic servants.

The milk-borne cases which are cited were traced, in practically every instance, to a carrier employed in the preparation or distribution of the milk. A number of milk epidemics are reviewed.

In the consideration of one milk-borne epidemic Scheller thought that he had proved the existence of a type of carrier in whom the typhoid bacillus existed as a true saprophyte. He called this type the "typhusbazillenzwischenträger" or intermediate carrier. A high incidence of typhoid fever had existed among persons employed at a particular dairy and among those who consumed the milk from

it. Fourteen persons who either worked in the dairy or consumed milk from it were found to be eliminating typhoid bacilli in the stools or in the urine. One of these, a female employee at the dairy, gave a history of an attack of typhoid 17 years before; the 13 others had never had typhoid fever and were healthy at the time. The following test was made: The female carrier was discharged from her dairy work and all were required to wash their hands with lysol before milking. The urinary carriers were given urotropin. At the end of a month the excreta of the 13 was examined and found to be free of typhoid bacilli, but the female carrier with the typhoid history was still eliminating bacilli. Scheller concludes that this woman was the true carrier and that the others were only temporary or intermediate carriers.

Lentz holds the view that carriers such as these are persons who have had slight or unnoticeable symptoms of typhoid fever or are what he calls "symptomless" typhoid fever cases, as he has found the agglutination reaction positive in such cases with the same serum dilutions as in clinically typical typhoid fever cases. Scheller, however, found in some of his cases that the agglutination reaction was negative, while in others the titre was 1 in 2,000.

The author gives a number of instances of the discovery of carriers in institutions and in bodies of troops which have been reported in the literature. They are all accounts of the discovery of carriers after some high incidence of typhoid fever, and will not be given here.

DIAGNOSTIC METHODS EMPLOYED IN SEARCHING FOR CARRIERS.

1. *The Widal reaction.*—In searching for carriers, in an institution for instance, a preliminary Widal test made on suspected persons may give line on a carrier. Although the Widal can not be entirely relied upon, Kayser states that 75 per cent of carriers give a marked Widal. Ledingham thinks this percentage too high, if 1 in 100 be taken as the lowest dilution for a positive result. Kamm found that four samples of blood from an asylum gave positive Widals, but he was unable to find the typhoid bacillus in the excreta of any one of the four persons who gave a positive Widal. Eccard has found that, in some persons who give no Widal or a positive one with low dilutions, the titre may suddenly jump to 1 in 100 with the appearance of symptoms of a gastrointestinal disturbance. After the attack the titre falls.

2. *Bacteriological methods.*—When carriers are being sought for and when facilities are at hand the best method of procedure is to make systematic bacteriological examinations of the excreta, beginning with persons who give a typhoid fever history or who present symptoms of gall bladder troubles. Widal tests should be applied at the same time and special attention given to persons showing a positive Widal reaction.

The method of isolating the typhoid bacillus is outlined briefly. Make a broth emulsion of two or three large loopfuls of feces and allow to sediment for an hour. Two or three small loopfuls of the emulsion are spread with a bent glass rod over the surface of the medium, which has been previously poured into Petri dishes and allowed to harden. The medium should be quite dry. After 24 hours the colorless suspicious typhoid colonies are fished and

inoculated into mannite-peptone-water. The typhoid bacillus produces acid but no gas in this medium, as also does the Flexner type of the dysentery bacillus. The typhoid bacillus can now be identified by the application of fermentation and agglutination tests.

The author gives a list of different media in current use for the isolation of the typhoid bacillus and suggests that better results can be obtained by learning thoroughly the use of one medium than by changing from one to another. These different media will be merely mentioned here:

1. Bile-salt-neutral-red-agar (MacConkey, Grünbaum and Hume).
2. Lactose-litmus-nutrose-kristalviolet-agar (Drigalski and Conradi).
3. Lactose-fuchsin-sodium-sulphite-agar (Endo).
4. Preliminary enrichment by caffeine before plating on Drigalski-Conradi medium.
5. Media containing malachite-green:
 - (a) Malachite-green-nutrose-agar (Loeffler).
 - (b) Malachite-green-bile-agar (Loeffler).
 - (c) Malachite-green-sodium-sulphite-bile-agar (Padlewski).
 - (d) Malachite-green-safranin-reinblau media (Loeffler and others).
 - (e) Preliminary enrichment on malachite-green media and later plating on Drigalski-Conradi or Endo media (Lentz and Tietz).

The author gives a number of comparative results of workers who used the above media, which show great variation. The method of Lentz and Tietz seems to have yielded the best results in the hands of recent observers.

GENERAL QUESTIONS OF CARRIER INFECTIVITY—STATISTICAL DATA.

The transference of the typhoid bacillus from a carrier to a new host depends upon the rate of elimination of bacilli, upon the personal hygiene of the carrier, and upon numerous other factors. A successful infection of the new host depends upon the magnitude of the dose received, upon the degree of virulence of the organism, and upon the susceptibility of the new host. The size of the dose of typhoid bacilli received by the new host is probably the most important factor in determining whether a successful infection will result or not. As to the virulence of the strains isolated from carriers, the same variations are found to exist as in strains isolated from acute cases of typhoid fever. No marked difference in degree of virulence for guinea pigs has been found to exist between carrier strains and strains isolated from acute cases.

The observations by Ledingham on guinea pigs show that the virulence of the strain of a typhoid bacillus in the same carrier may vary. He suggests that the virulence may be reduced during the winter months. Scheller thinks that an avirulent strain may suddenly regain its virulence.

The susceptibility of the new host is a factor which does not lend itself to experimentation, and our knowledge of it must be obtained from observations of actual cases. The report of Scheller's "typhus-bazillenzwischenträger" seems to show that the typhoid bacillus can exist as a saprophyte in the human body. Such instances, as has been said, may be cases of "symptomless" typhoid fever. Cases are reported which seem to indicate that trauma, pregnancy, etc., may predispose to infection. Conradi calls attention to the fact that strangers who come within the radius of infection of a carrier are more liable to infection than others, apparently on account of a lack of immunity.

Davies and Walker-Hall think that only at certain seasons are secondary infections liable to result from a carrier, and that every carrier has a peculiar season of his own when he is most likely to cause secondary infections.

Statistical data.—Regarding the relative number of cases of typhoid fever which are due to carriers, Kayser, in an analysis of 505 cases, found that 9.5 per cent were due to carriers. Of 28 carriers discovered, 11 were known to have caused secondary infections in their neighborhood. Foster found that 20 per cent of his 386 cases were attributable to carriers. Frosch found that 4.11 per cent of 6,708 cases of typhoid fever were due to carriers, and in another series of contact infections he found that about one-fourteenth were due to carriers. Klinger found that 431 carriers had given rise to 351 cases of typhoid fever, 50 due to transitory, and 300 due to chronic carriers.

In considering these results it must be borne in mind that the carrier has received credit only for those cases infected by him directly, and it must be remembered that the importance of the carrier as a source of infection increases when those cases are considered which received their infection from his victims. The line of infections may be considered as a chain, the first link of which is the carrier himself.

IMMUNITY QUESTIONS IN CARRIERS.

The author states that from two-thirds to three-fourths of all chronic carriers give a positive Widal titre at least 1 in 50. Some have shown a titre of 1 in 2,000. No definite statement regarding the Widal in transitory carriers can yet be made, but agglutinins have been demonstrated in the serum of persons who discharged typhoid bacilli for only a short while. It has been noted that the serum of a carrier may agglutinate the laboratory strain and not the homologous strain at all or may give only a late reaction with the homologous strain. In some cases vaccination raises the titre of the serum, in others not.

The few observations made on the bacteriocidal properties of the sera of carriers show little or no variation from the normal. Ledingham and also Gaehtgens have found a marked increase in the opsonin content of carrier sera. Hamilton recommends this procedure as a preliminary test in searching for carriers. Several observers have demonstrated the presence of complement-deviating substances in the sera of carriers who gave negative Widals.

METHODS TO DIMINISH THE SPREAD OF INFECTION BY CARRIERS.

A routine bacteriological examination of the excreta of convalescents should be made in order to determine the time when they ceased discharging typhoid bacilli. When a carrier is discovered, suitable treatment should be instituted in the way of diet and otherwise, in order to encourage the elimination of all the typhoid bacilli and if possible to avoid the chronic stage. Otto Mayer has suggested the foundation of a convalescent home for recovered typhoid cases, where examinations could be made and carriers discovered.

In asylums and other institutions isolation is the simplest procedure. All carriers should be under supervision, and should not be allowed to engage in any work necessitating them to handle or to

prepare food. All carriers should have individual articles which they use in their everyday life, such as dishes, basins, towels, etc. Toilets used by carriers should receive regular and systematic disinfection and carriers should be required to disinfect their hands after each visit to the toilet. Thorough washing with soap and water suffices in carriers of some occupations, but if there is a possibility of the carrier handling foodstuffs an antiseptic solution should be used in addition. Gaehtgens finds alcohol in the form of eau de cologne or spirits of wine the most satisfactory disinfectant.

The typhoid station at Strassburg, one of the stations in southwest Germany, issues a pamphlet which explains the carrier state and the danger of a carrier to the community, and gives full directions for carriers. Davies and Walker-Hall have issued a pamphlet of instruction to typhoid convalescents in which is explained the necessity for cleanliness and for strict personal hygiene. General hygienic measures are of great importance, in view of the lack of any sure method of preventing or of doing away with the carrier state.

CONCLUSION.

Dr. Ledingham has brought together in his interesting and instructive article a great mass of material, and has presented many facts not generally known concerning typhoid fever and concerning the typhoid bacillus carrier. The article is rather long and contains so many individual reports and statistics that many details have been omitted in this review.

The writer of this abstract wishes to state that for clearness and exactness he has used, in many places, the exact words and phrases used in the article itself. Anyone wishing more detailed information on the subject of the typhoid bacillus carrier is referred to Dr. Ledingham's report, where a rather full bibliography may be found.